CLAIMS

1. Method to produce an IL-11 agonist, which comprises producing a protein having the sequence of an IL-11 mutein that is derivable from a wild-type IL-11 sequence by replacement of at least two non-hydrophobic amino acids within the epitope for IL-11Rα by hydrophobic ones.

2. IL-11 mutein, the sequence of which comprises a sequence which is derivable from the complete sequence of a wild-type IL-11:

- by replacement of the hydrophilic amino acids at positions 182 and 186 (positions computed by reference to the complete wild-type sequence) by X_1 and X_2 respectively, X_1 and X_2 being chosen from the group comprising:
  - Valine (symbol = V or Val),
  - Alanine (symbol = A or Ala),
  - Proline (symbol = P or Pro),
  - Leucine (symbol = L or Leu),
  - Isoleucine (symbol = I or Ile),
  - Phenylalanine (symbol = F or Phe),
  - Methionine (symbol = M or Met), and
  - Tryptophan (symbol = W or Trp),
- and by deletion of a N-terminal portion that does not exceed the first 34 N-terminal amino acids.

3. IL-11 mutein of claim 2, characterized in that said wild-type IL-11 has the sequence of a human IL-11, or of a macaque IL-11, or of a mouse IL-11, or of a rat IL-11.

4. IL-11 mutein of claim 2 or 3, the sequence of which comprises a sequence chosen from the group comprising SEQ ID NO:9, SEQ ID NO:24, SEQ ID NO:39, SEQ ID NO:54, and the conservative variant sequences thereof, wherein said conservative variant sequences are of at least 80%, preferably at least 90% identity with at least one of SEQ ID NO:9, SEQ ID NO:24, SEQ ID NO:39, or SEQ ID NO:54, provided that X_1

and X_2 are still as defined in claim 2, and provided that the resulting variant protein has retained the ability to induce proliferation of an IL-11 dependent cell line.

5. IL-11 mutein according to any one of claims 2-4, characterized in that X1 and X2 are V or A.

6. IL-11 mutein according to any one of claims 2-5, characterized in that X1=V and X2=A.

7. IL-11 mutein of claim 6, characterized in that it comprises a sequence of SEQ ID NO:10, or of SEQ ID NO:25, or of SEQ ID NO:40, or of SEQ ID NO:55.

8. IL-11 mutein according to any one of claims 2-5, characterized in that X1=A and X2=V.

9. IL-11 mutein of claim 8, characterized in that it comprises a sequence of SEQ ID NO:11, of SEQ ID NO:26, of SEQ ID NO:41, or of SEQ ID NO:56.

10. IL-11 mutein according to any one of claims 2-5, characterized in that X1=V and X2=V.

11. IL-11 mutein of claim 10, characterized in that it comprises a sequence of SEQ ID NO:12, of SEQ ID NO:27, of SEQ ID NO:42, or of SEQ ID NO:57.

12. IL-11 mutein according to any one of claims 2-5, characterized in that X1=A and X2=A.

13. IL-11 mutein of claim 12, characterized in that it comprises a sequence of SEQ ID NO:13, of SEQ ID NO:28, of SEQ ID NO:43, or of SEQ ID NO:58.

14. IL-11 mutein according to any one of claims 2-13, characterized in that it comprises a sequence which is derivable from the complete sequence of a wild-type IL-11:

- by replacement of the hydrophilic amino acids in positions 182 and 186 (positions computed by reference to the complete wild-type sequence) by X_1 and X_2 respectively, X_1 and X_2 being as defined in claim 2, and

- by deletion of the first 21 N-terminal amino acids.

15. IL-11 mutein according to claim 14, characterized in that it comprises a sequence of SEQ ID NO:14, SEQ ID NO:29, SEQ ID NO:44 or SEQ ID NO:59, wherein X_1 and X_2 are defined in claim 2.

16. IL-11 mutein according to claim 15, characterized in that X_1=V and X_2=A.

17. IL-11 mutein according to claim 16, characterized in that it comprises a sequence of SEQ ID NO:15, or of SEQ ID NO:30, or of SEQ ID NO:45, or of SEQ ID NO:60.

18. IL-11 mutein according to claim 15, characterized in that X_1=A and X_2=V.

19. IL-11 mutein according to claim 16, characterized in that it comprises a sequence of SEQ ID NO:16, or of SEQ ID NO:31, or of SEQ ID NO:46, or of SEQ ID NO:61.

20. IL-11 mutein according to claim 15, characterized in that X_1=V and X_2=V.

21. IL-11 mutein according to claim 20, characterized in that it comprises a sequence of SEQ ID NO:17, or of SEQ ID NO:32, or of SEQ ID NO:47, or of SEQ ID NO:62.

22. IL-11 mutein according to claim 15, characterized in that X_1=A and X_2=A.

23. IL-11 mutein according to claim 22, characterized in that it comprises a sequence of SEQ ID NO:18, or of SEQ ID NO:33, or of SEQ ID NO:48, or of SEQ ID NO:63.

24. IL-11 mutein according to any one of claims 2-23, characterized in that it comprises a sequence which is derivable from the complete sequence of a wild-type IL-11, by replacement of the hydrophilic amino acids in positions 182 and 186 (positions

computed by reference to the complete wild-type sequence) by X_1 and X_2 respectively, X_1 and X_2 being as defined in claim 2.

25. IL-11 mutein according to claim 24, characterized in that it comprises a sequence of SEQ ID NO:19, or of SEQ ID NO:34, or of SEQ ID NO:49, or of SEQ ID NO:64, wherein X_1 and X_2 are as defined in claim 2.

26. IL-11 mutein according to claim 24, characterized in that X_1=V and X_2=A.

27. IL-11 mutein according to claim 26, characterized in that it comprises a sequence of SEQ ID NO:20, or of SEQ ID NO:35, or of SEQ ID NO:50, or of SEQ ID NO:65.

28. IL-11 mutein according to claim 24, characterized in that X_1=A and X_2=V.

29. IL-11 mutein according to claim 28, characterized in that it comprises a sequence of SEQ ID NO:21, or of SEQ ID NO:36, or of SEQ ID NO:51, or of SEQ ID NO:66.

30. IL-11 mutein according to claim 24, characterized in that X_1=V and X_2=V.

31. IL-11 mutein according to claim 30, characterized in that it comprises a sequence of SEQ ID NO:22, or of SEQ ID NO:37, or of SEQ ID NO:52, or of SEQ ID NO:67.

32. IL-11 mutein according to claim 24, characterized in that X_1=A and X_2=A.

33. IL-11 mutein according to claim 32, characterized in that it comprises a sequence of SEQ ID NO:23, or of SEQ ID NO:38, or of SEQ ID NO:53, or of SEQ ID NO:68.

34. Nucleic acid, characterized in that its sequence codes for a mutein according to any one of claims 2-33.

35. Nucleic acid according to claim 34, characterized in that it comprises the sequence of SEQ ID NO:72, wherein each of $n_1n_2n_3$ and $n_4n_5n_6$ codes for:

- Valine (symbol = V or Val), or
- Alanine (symbol = A or Ala), or
- Proline (symbol = P or Pro), or
- Leucine (symbol = L or Leu), or
- Isoleucine (symbol = I or Ile), or
- Phenylalanine (symbol = F or Phe), or
- Methionine (symbol = M or Met), or
- Tryptophan (symbol = W or Trp).

36. Nucleic acid according to any one claims 34-35, characterized in that it comprises the sequence of SEQ ID NO:72, wherein $n_1n_2n_3$ and $n_4n_5n_6$ are both selected from the group comprising the following codons:

- GCT, GCC, GCA, GCG,
- GTT, GTC, GTA, GTG,
- TTA, TTG, CTT, CTC, CTA, CTG,
- ATT, ATC, ATA,
- TTT, TTC,
- ATG,
- CCT, CCC, CCA, CCG,
- TGG.

37. Nucleic acid according to any one of claims 34-36, characterized in that it comprises the sequence of SEQ ID NO:71 or of SEQ ID NO:70, wherein the codons $n_1n_2n_3$ and $n_4n_5n_6$ are as defined in any one of claims 35-36.

38. Nucleic acid according to any one of claims 34-36, characterized in that it comprises the sequence of SEQ ID NO:76 or of SEQ ID NO:74, wherein the codons $n_1n_2n_3$ and $n_4n_5n_6$ are as defined in any one of claims 35-36.

39. Nucleic acid according to any one claims 34-35, characterized in that it has the RNA sequence of SEQ ID NO:75, wherein the codons $n_1n_2n_3$ and $n_4n_5n_6$ are both selected from the group comprising the following codons:

- GCU, GCC, GCA, GCG
- GUU, GUC, GUA, GUG,
- UUA, UUG, CUU, CUC, CUA, CUG,
- AUU, AUC, AUA,
- UUU, UUC,
- AUG,
- CCU, CCC, CCA, CCG,
- UGG.

40. Transfection vector, characterized in that it comprises a nucleic acid according to any one of claims 34-39.

41. Transfection vector according to claim 40, characterized in that it further comprises a nucleotide sequence coding for a Flag tag.

42. Transfection vector according to any one of claims 40-41, characterized in that it comprises the sequence of SEQ ID NO:79, wherein $n_1n_2n_3$ and and $n_4n_5n_6$ are as defined in claim 35.

43. Cell, characterized in that it comprises a nucleic acid according to any one of claims 34-39, and/or which has been transfected by a tranfection vector according to any one of claims 40-42, and/or which express a mutein according to any one of claims 2-33.

44. Drug characterized in that it comprises:

- a therapeutically effective amount of an IL-11 mutein according to any one of claims 2-33, or of a nucleic acid according to any one claims 34-39, or of a transfection vector according to any one of claims 40-42, or of a cell according to claim 43,
- and, optionally, a pharmaceutically-acceptable vehicle.

45. Drug according to claim 44, characterized in that it is intended for the prevention or treatment of an inflammatory disease or condition.

46. Drug according to any one claims 44-45, characterized in that it is intended for the prevention or treatment of a septic shock.

47. Drug according to any one claims 44-45, characterized in that it is intended for the prevention or treatment of diabetes.

48. Drug according to any one claims 44-47, characterized in that it is intended for inhibiting microvascular endothelium apoptosis.

49. Drug according to claim 44, characterized in that it is an anti-thrombocytopenia drug.